REMARKS

This Response is being filed in connection with the Office Action mailed May 29, 2003. Claims 16 to 20 are pending. Claims 16 and 17 stand withdrawn from consideration as directed to a non-elected invention. New claims 21 to 25, directed to the elected invention of predicting therapeutic efficacy of treatment of a multiple sclerosis, have been added. Accordingly, upon entry of the Response claims 18 to 25 are under consideration.

Regarding the Amendments to the Specification

The specification has been amended to address various informalities. In particular, sequence identifiers (SEQ ID NO) have been corrected or inserted at pages 5, 12, 13, 15 and 16. In addition, trademarks have been capitalized. Replacement sheets for Figures 11A-11D are submitted herewith, and the specification has been amended where Figure 11 is referenced to recite upper case letters, A-D. Thus, as the amendments to the specification were made to address various informalities, no new matter has been added and entry thereof is respectfully requested.

Regarding the Claim Amendments

The claim amendments are supported throughout the specification or were made to address various informalities. In particular, the amendment to claim 18 to recite that treatment is with a peptide of from "7 to 45" amino acids is supported, for example, at page 12, lines 10-14, which discloses the smallest common region of the effective decapeptides is from amino acid 87 to 93, and a seven residue peptide having the formula R_1-Val-His-Phe-Phe-Lys-Asn-Ile-R_2; and at page 14, lines 17-21, which discloses peptides effective in down regulating anti-MBP that "correspond to the amino acid sequence of h-MBP from about residue 61 to about 106," which is 46 amino acids in length. Claims 19 and 20 have been amended to depend from claim 18 instead of claims 1 to 3 due to incorrect claim numbering in the Preliminary Amendment filed November 30, 2001, and the elected invention. The amendment to claims 18 and 19 to recite the term "human leukocyte antigen" for the abbreviation HLA was made in response to the

Examiner's request. The amendment to claim 20 to recite the term "multiple sclerosis" for the abbreviation MS was also made in response to the Examiner's request. Thus, as the amendments to the claims were made to address various informalities, no new matter has been added and entry thereof is respectfully requested.

Regarding the New Claims

New claims 21 to 25, directed to methods of predicting therapeutic efficacy of treatment of a multiple sclerosis patient with particular peptides in part included in claim 18, by screening a multiple sclerosis patient for the presence of an human leukocyte antigen (HLA)-DR2 haplotype, are supported throughout the specification. In particular, claim 21 is supported as set forth above for the amendment to claim 18 and, for example, at page 42, line 1, to page 43, line 11, which discloses DR2 haplotypes of patients who have low or undetectable auto-antibody levels one year after a second iv MBP injection. Claim 21 is also supported, for example, at page 14, line 17, to page 15, line 6. Claims 22 and 23 are supported, for example, by claim 18. Claims 24 and 25 are supported, for example, at page 12, lines 11-26, and as set forth above for claim 21. Thus, as claims 21 to 25 are supported throughout the specification, no new matter has been added and entry thereof is respectfully requested.

Regarding the Filing Date and Priority Claim

The claim of priority of the subject application to U.S. Application Serial No. 09/055,263, now U.S. Patent No. 6,252,040, was objected to for allegedly lacking copendency between the subject application and the parent application. An incorrect filing date accorded to the subject application by the Patent Office is relied upon as grounds for this objection.

The filing date of the subject application is March 20, 2001. A brief chronology of events that lead the Patent Office to accord an incorrect filing date to the subject application follows. A Notice of Incomplete Non-Provisional Application was mailed by the Patent Office on November 29, 2001, alleging that no drawings were filed. In response, a Petition for Review of Notice of Incomplete Non-Provisional Application was filed on January 11, 2002, including

evidence that the Drawings had been filed March 20, 2001. Submitted with the Petition was a copy of the date-stamped return post-card indicating that Figures 1-18 were filed with the application on March 20, 2001. Unfortunately, although this Petition was timely received by the Patent Office (the Patent Office deducted the Petition fee from the deposit account), it has to date not been acted upon. Applicants have been in contact with the Petitions branch of the Patent Office and understand that the Petition for correcting the error in the filing date of the subject application is presently being acted upon.

Applicants also wish to bring to the Examiner's attention the fact that parent application serial no. 09/055,263 was expressly incorporated by reference in the subject continuation application at the time the subject application was filed (see the Rule 53(b) request for filing sheet submitted with the subject application March 20, 2001, attached herewith as Exhibit A). Item #3 of the request states that "The entire disclosure of the prior application is considered as being a part of the disclosure of the accompanying application and is hereby incorporated therein by reference thereto." Accordingly, as Figures 1 to 18 of the parent application are a part of the subject application filed on March 20, 2001, for this reason alone the subject application is entitled to the March 20, 2001, filing date.

In view of the foregoing, the subject application is entitled to a March 20, 2001, filing date. Because the subject application was filed prior to the issuance of the patent from parent application serial no. 09/055,263, the subject application's claim to the priority of application serial no. 09/055,263 under 35 U.S.C. §120 is proper.

Regarding the Drawings

The Drawings stand objected to due to absence of a capital letter in Figure 11. Submitted herewith is replacement sheets for Figure 11 in which lower case letters (a-d) have been replaced with upper case letters (A-D). In addition, the specification has been amended to reflect the change in letter case. Accordingly, in view of replacement Figure 11 and the amendments to the specification, the Drawings are in compliance with 37 C.F.R. §1.84, and particularly 37 C.F.R. §1.84(u)(1).

Regarding the Specification and Sequence Listing

The application allegedly fails to comply with the requirements for applications with sequences under 37 C.F.R. §§1.821-1.825. The Examiner requests that the sequences be identified and, if necessary, that substitute paper and computer readable copies of the Sequence Listing, and an amendment directing entry into the application, be submitted.

Applicants have amended the specification to insert sequence identifiers (SEQ ID NOs) as set forth above. In addition, submitted herewith are substitute paper and computer readable copies of the Sequence Listing under 37 C.F.R. §1.825. The substitute paper and computer readable copies of the Sequence Listing are identical and do not introduce new matter. An executed statement under 37 C.F.R. §§1.821(f) and (g) to that effect is submitted herewith.

The substitute Sequence Listing including the 170 amino acid human myelin basic protein (MBP) as SEQ ID NO:1 does not add new matter because, *inter alia*, this amino acid MBP sequence was disclosed in parent application serial no. 09/055,263 (now U. S. Patent No. 6,252,040; see column 25, SEQ ID NO:1), which was expressly incorporated by reference in the subject application (see the Rule 53(b) request for filing sheet, Item #3, attached herewith as Exhibit A). Accordingly, as the 170 amino acid MBP sequence of the parent application was a part of the subject application filed on March 20, 2001, inclusion of this MBP sequence in the substitute Sequence Listing does not introduce new matter. Thus, as the substitute Sequence Listing does not introduce new matter, entry thereof is respectfully requested.

Regarding the Claim Objections

Claims 19 and 20 stand objected to due to depending from claims 1 and 3. Applicants have amended claims 19 and 20 to depend from claim 18, due to the erroneous claim numbering submitted with the Preliminary Amendment filed November 30, 2001. In view of the amendment, Applicants respectfully request that the objection to claims 19 and 20 be withdrawn.

I. REJECTIONS UNDER 35 U.S.C. §112

The rejection of claims 18 to 20 under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement is respectfully traversed. The grounds of rejection relate to 1) the alleged absence of a peptide from the specification; and 2) the recitation of "substitutions, additions or deletions" in the claims. As to the latter, allegedly the specification "fails to provide an adequate enabling disclosure for practicing such method of treatment."

Claims 18 and 20 are adequately enabled by the specification. Applicants first wish to point out that the subject application describes the full length human MBP protein, which is set forth as SEQ ID NO:1 in the sequence listing. Thus, the grounds for rejection due to the absence of this peptide from the specification should properly be withdrawn.

As to the second grounds of rejection, the preamble of claims 18 to 20 and 22 recite "predicting therapeutic efficacy of treatment of a multiple sclerosis patient with a peptide of from 7 to 46 (claims 18 to 20) or 8 to 25 (claim 22) amino acids and having a sequence contained within amino acid residues 61-106 of SEQ ID NO:1, including substitutions, additions or deletions thereof." The body of these claims recite how the method is performed, in particular, "screening a multiple sclerosis patient for the presence of an human leukocyte antigen (HLA)-DR2 haplotype, wherein the presence of the human leukocyte antigen (HLA)-DR2 haplotype in the patient is predictive of therapeutic efficacy of treatment with the peptide." Thus, claims 18 to 20 and 22 do not require treatment of a multiple sclerosis patient. In fact, no treatment at all is being claimed. Thus, as treatment of a multiple sclerosis patient is not being claimed, treatment of a multiple sclerosis patient need not be enabled. As such, the grounds for rejection due to the allegation that the specification "fails to provide an adequate enabling disclosure for practicing such method of treatment," is improper and must be withdrawn.

As set forth in the claims, the method is performed by screening a multiple sclerosis patient for the presence of an human leukocyte antigen (HLA)-DR2 haplotype. Identifying an (HLA)-DR2 haplotype in such a patient in turn predicts therapeutic efficacy. Accordingly, it is the screening for the presence of an human leukocyte antigen (HLA)-DR2 haplotype that must satisfy the enablement requirement under 35 U.S.C. §112, first paragraph. In this regard, (HLA)-

DR2 haplotypes including, for example, DRB1*1501 and DRB1*15021, were known in the art at the time of the invention. Identifying the presence of these and other (HLA)-DR2 haplotypes can be performed by methods known in the art at the time of the invention.

In sum, as screening for an human leukocyte antigen (HLA)-DR2 haplotype was known in the art at the time of the invention, the claims are adequately enabled. As such, the rejection under 35 U.S.C. §112, first paragraph must properly be withdrawn.

The rejection of claims 18 to 20 under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is respectfully traversed. The Examiner indicates that claims 18-20 allegedly "fail(s) to correspond in scope with that which applicant(s) regards as the invention." The claims have also been rejected due to several allegedly indefinite terms.

Applicants first respectfully direct the Examiner's attention to M.P.E.P. §2173.02, particularly that "[t]he examiner's focus during examination of claims for compliance with....35 U.S.C. §112, second paragraph is whether the claim meets the threshold requirements of clarity and precision, not whether more suitable language or modes of expression are available." [Emphasis added] Furthermore, "latitude in the manner of expression and the aptness of terms should be permitted." The determining factors is "whether the claim apprises one of ordinary skill in the art of its scope." *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379 (Fed. Cir. 2000)

Here, claims 18 to 20 are clear and definite as originally filed because the skilled artisan would be apprised of the claimed subject matter. In particular, as to the nature of SEQ ID NO:1, this sequence identifies this 170 amino acid human myelin basic protein (MBP) in the substitute Sequence Listing submitted herewith. As discussed above, the substitute Sequence Listing including the 170 amino acid MBP does not introduce new matter because, *inter alia*, this MBP sequence was disclosed in the parent application, which was expressly incorporated by reference in the subject application (see Exhibit A). As such, claims 18-20 correspond in scope with that which applicant(s) regards as the invention.

As to the various abbreviations, in view of the specification and knowledge in the art the skilled artisan would understand the meaning of the abbreviations used. In particular, in view of the specification the skilled artisan understands that the abbreviation "MS" means "multiple sclerosis," and in view of the art that "HLA" means "human leukocyte antigen." The skilled artisan also understands that in the relevant art "DR" refers to an HLA class II subregion where such antigens are located (see, for example, Harrison's "Principles of Internal Medicine," McGraw-Hill, New York). Polymorphisms are known to occur in DRs, and the skilled artisan also knows that DRB1*1501 and DRB1*15021 refer to particular class II polymorphic alleles. Thus, given that the skilled artisan understands the meaning of "MS," "HLA," "DR," "DRB1*1501" and "DRB1*15021," claims 18 to 20 are clear and definite as originally filed.

In any event, solely in an effort to comply with the Examiner's request, and not because any of the terms are in any way vague or indefinite, claim 20 has been amended for reasons unrelated to patentability to recite "multiple sclerosis," and claims 18 and 19 have been amended to recite "human leukocyte antigen." Because the meaning of "DR" and the "DRB1*1501" and DRB1*15021" polymorphisms are understood by the skilled artisan, and their meaning cannot be conveniently conveyed by other language, Applicants need not amend the claims in this respect to satisfy 35 U.S.C. §112, second paragraph.

As to the term "about," the Federal Circuit has held that including terms of degree does not automatically render the claim indefinite. *Seattle Box Co., v. Industrial Crating & Packing*, Inc. 731 F.2d 818 (Fed. Cir. 1984). In this regard, the skilled artisan, in view of the specification, would understand the meaning of the term "about" in the context of amino acid length. For example, the specification discloses that the peptides can vary by single amino acid increments, and in one embodiment, the peptide can be a 26 amino acid residue (see, for example, page 13, lines 12-13, and lines 17-18). Thus, in view of this disclosure, the skilled artisan would know that the phrase "about 8 to about 25 amino acids" would include peptides having 7 or 26 amino acids.

In any event, solely in an effort to comply with the Examiner's request, and not because the term "about" is in any way vague or indefinite, claim 18 has been amended for reasons

unrelated to patentability to delete the term "about." Accordingly, in view of the amendment, this grounds for rejection are moot.

In sum, in view of the fact that one skilled in the art would understand the meaning of the various terms used in claims 18 to 20 and, therefore, be apprised of the scope of the claims, the claims are clear and definite. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph, be withdrawn.

II. REJECTION UNDER 35 U.S.C. §102(a)

The rejection of claims 18 to 20 under 35 U.S.C. §102(e) as allegedly anticipated by Gaur *et al.* (U.S. patent No. 6,379,670) is respectfully traversed.

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration (In re Spada, 15 USPQ 2d 1655 (Fed. Cir. 1990), In re Bond, 15 USPQ 2d 1566 (Fed. Cir. 1990).

As set forth above, the subject application was filed March 20, 2001, and is a continuation of application Serial No. 09/055,263, filed April 6, 1998. As such, the subject application has an earlier priority date than Gaur *et al.* (U.S. Patent No. 6,379,670, filed August 19, 1999) and, therefore, Gaur *et al.* (U.S. Patent No. 6,379,670) is not available as prior art under 35 U.S.C. §§102 or 103 against the claims of the subject application. Accordingly, the rejection under 35 U.S.C. §102(e) must properly be withdrawn.

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 18 to 25 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 509-4065.

Please charge any additional fees, or make any credits, to Deposit Account No. 03-3975.

Respectfully submitted,

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